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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/777,838	WEDEL ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 7-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 7-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on February 28, 2008.

Currently, claims 1-3 and 7-24 are under examination on the merits.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Response to Arguments

Applicant's arguments (see pages 5-10) and the declaration under 37 CFR §1.131, filed on February 28, 2008, with respect to the rejection(s) of claim(s) 1-3 and 7-24 under PR Newswire have been fully considered and are persuasive. Therefore, the rejections based on the PR Newswire reference have been withdrawn. However, upon further consideration, a new ground(s) of rejection is made. See below.

New Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 and 7-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennett et al. (US 6,096,722) in view of Knobler et al. (*The American Journal of Gastroenterology,* 1986, 81:199-201), Madden et al. (*Gut,* 1990, 31:247-249), Subramani et al. (*Gut,* 1993, 34:1539-1542), and Patel et al. (citation of record).

The claims are drawn to a method of treating pouchitis in a patient comprising rectally administering a pharmaceutical composition known as ISIS 2302, wherein the composition is formulated for rectal use, wherein ISIS 2302 is an antisense oligonucleotide targeted to ICAM-1 (see page 20 of the specification).

Bennett et al. teach a method of making enema formulations of ISIS 2302 for rectal administration, wherein some pre-clinical studies have shown that ISIS 2302 given by enema demonstrated good tolerability and tissue uptake. See Examples 46 and 55. They teach that such formulations distribute ISIS 2302 to the targeted colonic tissue of animals, demonstrating the bioavailability of the oligonucleotide of ISIS 2302 in the targeted tissue. See Examples 47-48. They further teach that a pharmaceutical composition comprising ISIS 2302 can be formulated as suppositories and enemas for rectal use. See column 18, lines 13-27. They report that human clinical trials of ISIS 2302 have revealed that the ISIS 2302 compound is safe and its *in vivo* pharmacokinetics in human subjects are promising for future use. See Example 50. They further teach that ISIS 2302 has been evaluated up to Phase II trials for patients with Crohn's disease and ulcerative colitis, where in said ISIS 2302 has consistently demonstrated desired therapeutic efficacy. See Examples 51-55. See also claims 9-11 and 16-19, which are drawn to methods of treating a human having inflammatory bowel disease or ulcerative colitis, or Crohn's disease, comprising administering a therapeutic amount of ISIS 2302 by formulating said ISIS 2302 in a penetration enhancer. They further teach that ICAM-1 inhibitors are useful for treating various inflammatory disorders of the bowel in an animal, wherein such disorders include, for example, gastrointestinal diseases such as inflammatory bowel disease, ulcerative colitis, Crohn's disease, and other forms of regional enteritis. See column 3, lines 32-49; column 21, lines 54-65. Bennett et al. do not teach applying their therapeutic methods to treating pouchitis.

Knobler et al. teach that the inflammation in the ileal pouch of a pouchitis patient resemble that of ulcerative colitis both clinically and histologically, wherein the pouchitis patient originally suffered from ulcerative colitis and underwent total colectomy and a continent

ileostomy, which constructed a continent ileal pouch. They further report that symptoms of pouchitis were observed almost exclusively in patients who underwent colectomy for ulcerative colitis and Crohn's disease. Based on their own observation a patient and the clinical reports by others, they suggest that pouchitis is a recurrence of patient's original inflammatory bowel disease and not a local process. They further exemplify a pouchitis patient who was treated with steroid enemas. See the entire reference.

Madden et al. teach that pouchitis is confined to patients operated on for ulcerative colitis and that severe acute inflammatory changes in pouchitis patients are more common in ulcerative colitis (UC) patients (pages 247-248). Indeed, they report that "unequivocal pouchitis has only been diagnosed in colitis patients" (page 248). They further teach that UC and pouchitis may have the same etiology (page 248). They teach that pouchitis remains an important clinical problem (page 248). They teach that pouchitis has been treated with enemas containing steroids or salicylic acid derivatives (page 248).

Concordant with the teachings of Knobler et al. and Madden et al., Subramani et al. teach that pouchitis is a complication of ileal pouches in ulcerative colitis and that inflammatory changes in pouchitis patients are seen almost exclusive in patients who have had colectomy for inflammatory bowel disease (pages 1539, 1542). They further teach that some immunologically vulnerable patients having inflammatory bowel disease, or Crohn's disease, or ulcerative colitis are prone to develop refractory pouchitis (page 1542).

Patel et al. teach that patients with pouchitis have a significantly high level of plasma ICAM-1. In fact, Patel et al. show that the plasma soluble ICAM-1 level is the highest in patients with pouchitis compared to patients with Crohn's disease or those with ulcerative colitis. They

also teach that plasma soluble ICAM-1 level is significantly increased during active inflammatory bowel disease and pouchitis. See the entire reference.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the therapeutic methods for treating inflammatory bowel disease, or Crohn's disease, or ulcerative colitis, comprising administering ISIS 2302 in an enema formulation for rectal use comprising a penetration enhancer of Bennett et al. to the treatment method of pouchitis.

With such a wealth of knowledge that pouchitis and UC have the same etiology and that pouchitis develops exclusively in UC patients and that pouchitis patients display higher expression levels of plasma ICAM-1 compared to UC patients, one of ordinary skill in the art would have been motivated to apply the therapeutic methods comprising administering ISIS 2302 of Bennett et al. to treat pouchitis patients. One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the claimed invention because the therapeutic efficacy of ISIS 2302 in an enema formulation for treatment of inflammatory bowel disease, Crohn's disease, and UC was known in the art as clearly taught and claimed in the Bennett et al. reference, and because the pathological etiology, symptoms, and treatment for pouchitis were known to be similar to those of inflammatory bowel disease, or Crohn's disease, or UC since early 1986. Note that all secondary references were published in the years between 1986 and 1995. As such, the belief in the clinical link between pouchitis and UC (or inflammatory bowel disease or Crohn's disease) had been faithfully maintained in the art for a decade. With such level of confidence, one of ordinary skill in the art would have been motivated to apply the therapeutic methods of Bennett et al. to another similar inflammatory disease, pouchitis. Since a particular

known technique, which is administering the ISIS 2302 compound in an enema form for rectal use for treatment of pouchitis-related inflammatory diseases, was recognized as part of the ordinary capabilities of one of ordinary skill in the art, the skilled artisan, with a reasonable expectation of success, would have been capable of applying said known technique to treat pouchitis by employing the same method steps taught by Bennett et al. Accordingly, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Claims 1-3 and 7-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gewirtz et al. (*Current Opinion in Investigational Drugs,* 2001, 2:1401-1406) in view of Madden et al. (*Gut,* 1990, 31:247-249), Subramani et al. (*Gut,* 1993, 34:1539-1542), and Patel et al. (citation of record).

The claims are described above.

Gewirtz et al. report the history of a particular ISIS Phamaceuticals' product known as ISIS 2302 or Alicaforsen, Which inhibits ICAM-1. See the entire reference. They teach that ICAM-1 has been known in the art to play a key role in mediating inflammation, and therefore ISIS 2302 has long been considered to have a therapeutic potential to treat a wide range of inflammatory disorders, including inflammatory bowel disease (IBD), Crohn's disease (CD), and ulcerative colitis (UC). To support this notion, they teach that ICAM-1 expression is elevated in chronic inflammatory disease states including IBD and therefore reduction of ICAM-1 expression by alicaforsen can "reasonably be expected to be therapeutic" for this disorder, based on the factual evidence that other pharmacological approaches to inhibit ICAM-1 via small molecule inhibitors and antibodies have "consistently" reduced the severity of inflammation in

animal models. See pages 1401-1402. They teach that, as of the publication of the Gewirtz et al. reference (that is, October 2001), ISIS 2302 has undergone phase II clinical trials and is undergoing phase III clinical trials. They further teach that the enema formulation of alicaforsen entered phase IIa clinical trials for UC in December 1999. Note that the term "enema" means "the injection of liquid into the intestine by way of the anus". See the dictionary citation. They expressly report their opinion that "There is a great need, and thus potentially a large market, for drugs that can treat CD. While targeting ICAM-1 has shown therapeutic potential for other disorders (e.g., arthritis), few inflammatory disorders are as lacking in therapeutics as CD…ICAM-1 is clearly an attractive pharmacological target for chronic inflammatory diseases in general…Should effective subcutaneous or enema dosing be established, alicaforsen would be considerably more desirable." See page 1403. Gewirtz et al. do not teach using alicaforsen (also known as ISIS 2302 in enema formulation for rectal use) to treat pouchitis.

Madden et al. teach that pouchitis is confined to patients operated on for ulcerative colitis and that severe acute inflammatory changes in pouchitis patients are more common in ulcerative colitis patients (pages 247-248). Indeed, they report that "unequivocal pouchitis has only been diagnosed in colitis patients" (page 248). They further teach that ulcerative colitis and pouchitis may have the same etiology (page 248). They teach that pouchitis remains an important clinical problem (page 248).

Concordant with the teachings of Madden et al., Subramani et al. teach that pouchitis is a complication of ileal pouches in ulcerative colitis and that inflammatory changes in pouchitis patients are seen almost exclusive in patients who have had colectomy for inflammatory bowel disease (pages 1539, 1542). They further teach that some immunologically vulnerable patients

having inflammatory bowel disease, or Crohn's disease, or ulcerative colitis are prone to develop refractory pouchitis (page 1542).

Patel et al. teach that patients with pouchitis have a significantly high level of plasma ICAM-1. In fact, Patel et al. show that the plasma soluble ICAM-1 level is the highest in patients with pouchitis compared to patients with Crohn's disease or those with ulcerative colitis. They also teach that plasma soluble ICAM-1 level is significantly increased during active inflammatory bowel disease and pouchitis. See the entire reference.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the therapeutic methods for treating inflammatory bowel disease, or Crohn's disease, or ulcerative colitis, comprising administering ISIS 2302 in an enema formulation for rectal use of Gewirtz et al. to the treatment method of pouchitis.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success, because alicaforsen enema was known to have a therapeutic potential to treat a wide range of inflammatory disorders, including inflammatory bowel disease (IBD), Crohn's disease (CD), and ulcerative colitis (UC) as taught by Gerwirtz et al., and because one of ordinary skill in the art would have seen the clinical, pathological, and etiological similarities between pouchitis and other bowel inflammatory disorders (e.g., IBD, CD, UC) as taught by Madden et al., Subramani et al., and Patil et al., and therefore would have seen the therapeutic benefit of alicaforsen enema for pouchitis treatment. Since all the knowledge and skills required to arrive at the claimed invention were within the technical grasp of one of ordinary skill in the art at the time of the invention, the claimed invention taken as whole would have been *prima facie* obvious at the time of filing.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 and 7-24 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 3 of U.S. Patent No. 6,169,079 B1 in view of Patel et al. (citation of record).

The reference claim recites, "A method of treating a human having a disease with an inflammatory component which is modulated by changes in human intercellular adhesion molecule-1 comprising contacting a human with a therapeutically effective amount of an antisense oligonucleotide of claim 1." The antisense oligonucleotide claimed in claim 1 is broadly drawn to a genus of various species of antisense oligonucleotides, which include those targeted to a 3'-untranslated sequence of an mRNA encoding human intercellular adhesion molecule-1.

Since the reference claim in 6,169,079 B1 expressly recites "treating human" with "a therapeutically effective amount of an antisense oligonucleotide", one of ordinary skill in the art would have searched for "therapeutically effective" antisense oligonucleotide targeted to "human" ICAM-1 by consulting the disclosure of the specification. Although the specification of 6,169,079 B1 lists 29 different SEQ ID NOs of antisense oligonucleotides targeted to "human" ICAM-1 (see Table 1), some were found to have no inhibitory activity, while some were found to have superior or improved antisense activity compared to others. See columns 18-19. Hence, although it is true that the antisense oligonucleotide claimed in claim 1 is so broad and generic in scope, the antisense oligonucleotide claimed in claim 3 does not necessarily read on "any" one of antisense oligonucleotides made under the sun. Since the claimed invention of claim 3 is expressly directed to a therapeutic method, any layperson would understand that an antisense oligonucleotide shown to have no effect at all would not be used in the claimed method.

Similarly, any person of ordinary skill in the art, or even a person having no knowledge of antisense oligonucleotides but having common sense or reasoning skills would have acknowledged that choosing an antisense oligonucleotide that has shown some inhibitory effect would be a logical, reasonable choice in order to use it to treat ICAM-1-related inflammatory diseases as claimed in claim 3. Among the handful of antisense oligonucleotides that have passed the screening test for their inhibitory antisense activity, the specification further teaches that ISIS 1939 and ISIS 2302, both of which are targeted to the 3'-UTR of "human" ICAM-1, markedly reduced ICAM-1 mRNA levels. See Examples 16 and 18. The specification of 6,169,079 B1 does not contain any *in vivo* working examples for any of the ICAM-1 antisense oligonucleotides targeted to "human" sequence. However, it provides working *in vivo* examples demonstrating therapeutic effects of ICAM-1 antisense oligonucleotide, wherein the working examples comprise an antisense oligonucleotide targeted to the 3'-UTR of mouse ICAM-1, which is identified as "ISIS 3082". See Examples 19-22.

In essence, therefore, the referenced claim method does not encompass countless possible species of antisense oligonucleotides claimed in claim 1. Rather, the "therapeutic" method in the reference claim only encompasses antisense oligonucleotides having therapeutic potential to treat diseases that are inflammatory in nature and are associated with ICAM-1 expression. Hence, unlike the method claimed in claim 2 of US 6,169,079 B1 (method drawn to inhibiting the synthesis of ICAM-1), the method claimed in the reference claim requires an antisense oligonucleotide useful in human, which confers a therapeutic effect of treating a human disease. As such, the scope of the claimed method in the reference claim embraces only those antisense oligonucleotides shown to have therapeutic potentials, albeit its recitation of "an antisense

oligonucleotide of claim 1". As stated above, only two human ICAM-1 antisense oligonucleotides were shown to have therapeutic potentials via both inhibitory screening tests and *in vitro* experimental data, and the murine counterpart having the *in vivo* therapeutic efficacy (ISIS 3082) is targeted to the 3'-UTR of the ICAM-1 gene, just like the two human antisense oligonucleotides, ISIS 1939 and ISIS 2302. Based on the factual evidence and teachings provided by the disclosure of US 6,169,079 B1, one of ordinary skill in the art would have reasonably delineated that either ISIS 1939 or ISIS 2302 would be the antisense oligonucleotide encompassed by the therapeutic method of the reference claim and therefore would have logically selected one of the two antisense compounds with a reasonable expectation of success.

To reiterate, in view of the foregoing, and in light of the claim limitations set forth in the reference claim (e.g., "therapeutically effective", "antisense oligonucleotide targeted to human ICAM-1", "treating human"), it would have been obvious to one of ordinary skill in the art to interpret the claimed antisense oligonucleotide used in the referenced method claim to be an antisense oligonucleotide targeted to the 3'-UTR of a human ICAM-1 mRNA sequence, simply by referring to the disclosure of the specification to identify a human antisense oligonucleotide having a therapeutic potential and would have successfully arrived at either ISIS 1939 or ISIS 2302 as the claimed antisense oligonucleotide used in the human treatment method of the reference claim. See *Sinclair & Carroll Co. v. Interchemical Corp.,* 325 U.S. at 335, 65 USPQ at 301: "Reading a list and selecting a known compound to meet known requirements is no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle." See also the recent Supreme Court decision in *KSR International CO. v. TELEFLEX INC.,* No. 04-1350 (U.S. Apr. 30, 2007), 82 USPQ2d 1385. At page 1390, the Court expressed "When there is a

design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." (emphasis added). Again, there is nothing unexpected or unobvious about selecting ISIS 1939 or ISIS 2302 for the therapeutic method claimed in claim 3, because either compound was the identified, predictable solution among the finite number of identified, predictable options within the technical grasp of one of ordinary skill in the art, and because such selection step would have been no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle.

The specification of 6,169,079 B1 also teaches that the pharmaceutical composition "may be administered in a number of ways", which include rectal route of administration in the form of suppositories. See column 9, lines 11-20.

Although the reference claim does not recite treatment of pouchitis *per se,* the reference claim broadly and expressly recites "treating a human having a disease with an inflammatory component which is modulated by changes in human intercellular adhesion molecule-1". Hence, it would have been obvious to one of ordinary skill in the art to apply the treatment method of human inflammatory disease of the reference claim to treat pouchitis as claimed in the instant case, with a reasonable expectation of success, because Patel et al. taught that patients with pouchitis have a significantly high level of plasma ICAM-1 compared to patients with Crohn's disease or those with ulcerative colitis and that the plasma soluble ICAM-1 level increases significantly during active pouchitis. Since ISIS 2302, one of the two antisense oligonucleotides shown to have therapeutic efficacy in the disclosure of 6,169,079, is targeted to human ICAM-1,

and since pouchitis is a human disease that shows a significantly increased level of ICAM-1 during active pouchitis, with a greater level of increase compared to patients having other inflammatory diseases associated with ICAM-1 such as Crohn's disease or ulcerative colitis, it would have flowed logically to one of ordinary skill in the art at the time the invention was made to apply the method of claim 3 of US 6,169,079 B1 to treat pouchitis in a human by formulating ISIS 2302 for rectal use. Accordingly, the claimed invention taken as a whole would have been *prima facie* obvious over the claimed invention in the reference claim in view of Patel et al., at the time of filing.

Claims 1-3 and 7-24 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9-11 and 16-19 of U.S. Patent No. 6,096,722 in view of Patel et al. (citation of record).

The reference claims are drawn to a method of treating an inflammatory disease comprising administering ISIS 2302 formulated in a penetration enhancer, wherein the inflammatory disease is a gastrointestinal disease including Crohn's disease and ulcerative colitis. Note that the expressly claimed SEQ ID NO:22 in claim 16 of US 6,096,722 is synonymous with ISIS 2302 and identical with the instantly claimed SEQ ID NO:1. The specification of 6,096,722 teaches that the pharmaceutical composition "may be administered in a number of ways", which include rectal route of administration in the form of suppositories. See columns 17-18. Although the reference claims do not recite treatment of pouchitis *per se,* it would have been obvious to one of ordinary skill in the art to use the methods in the reference claims to treat pouchitis with a reasonable expectation of success, because Patel et al. taught that

patients with pouchitis have a significantly high level of plasma ICAM-1 compared to patients with Crohn's disease or those with ulcerative colitis and that the plasma soluble ICAM-1 level increases significantly during active pouchitis. Since the methods of the reference claims are drawn to treating Crohn's disease and ulcerative colitis patients, who were known to have a high level of plasma ICAM-1, it would have been *prima facie* obvious to one of ordinary skill in the art to apply the referenced methods to treat pouchitis patients, who were known to have a significantly higher level of plasma ICAM-1 compared to those having Crohn's disease and ulcerative colitis patients.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/J. E. Angell/
Primary Examiner, Art Unit 1635